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Neurological Health Outcomes and Environmental Exposures

Background:

- Real public concern around prevalence of autism in the United States and desire to understand potential role of environmental factors.
- Recent high visibility research publications associating environmental factors and risk of autism spectrum disorder (ASD), and other neurological outcomes. Most noteworthy among them are:
    - Air pollution epidemiology: significant associations of increased ASD risk with air pollution exposure during gestation and/or early infancy (e.g., Von Ehrenstein 2014)
    - Toxicology: animal study suggesting mechanism for adverse neurological outcomes from exposures to concentrated ambient particles (CAPs) with potential relevance for ASD (Allen 2014)
    - Gene-Environment interactions: first demonstrations of a specific interaction between a well-established genetic risk factor and an environmental factor (air pollution) that independently contribute to autism risk (Volk, 2014)
- To date, research in this area has been limited and complexity of the exposures, ASD etiology, and health outcomes, make it difficult to evaluate and interpret associations with exposures to environmental chemicals.

Dilemma for EPA:

- Public demand for the EPA to address or mitigate these environmental factors.
- Evidence is building, but far from actionable.
- Need more efficient, effective approaches to develop understanding of biological basis of ASD and neurological disease to support intervention to prevent effects.

Purpose for this call

- Consult on opinions and perspectives on strengths and limitations of associations between ASD and environmental factors (air pollution, endocrine disrupting chemicals)
- What are the opportunities to advance scientific basis for regulation and other public health actions required to anticipate and prevent exposures to environmental factors with strong evidence of links to adverse neurological outcomes?
- Explore new partnership on cross-cutting, national-scale problem to develop tools, methods, and translational science required to support EPA and other public-health decision makers.
- Discuss formal EPA representation to IACC and relevant subcommittees
    - Recommend EPA Science Advisor and OCHP Director

Exploring New Partnerships

- EPA's historical investments in epidemiological studies (such as EPA-NIEHS funded Children's Centers) have identified some important associations and hypotheses.
- EPA 'big data' approaches – including research in computational toxicology, high throughput toxicity screening through Tox21 collaborations, adverse outcome pathways (AOPs) and virtual tissue modeling is advancing efficient methods for translating findings in biology to predict effects of environmental exposures and to support public-health decision making.
- **Discovery science (potential linkages with the BRAIN Initiative)**: partner with NIH (consider

model of Tox21) to examine potential interaction and impact of multiple stressors on ASD pathology and etiology, including understanding of impacts of chemical exposures on related intermediate endpoints. Some opportunities:

- Postulate adverse outcome pathways (AOPs) and AOP networks based on genetic risk factors of ASD and other neurological outcomes (e.g., leverage early results of 3-D brain mapping)
- Develop assays to cover biological endpoints relevant for linking molecular initiating events to neurological outcomes, screen chemicals for these endpoints
- Develop high-throughput methods that model gene-environment interactions for data driven hypothesis development
- Apply experimental models of ASD to explore gene-environment interactions (i.e., animal, stem cell systems)

- **Exposure science (potential linkages with sensors/apps/biomarkers research): p**artner with NIH and DARPA to advance methods to measure exposures directly and to incorporate exposure metrics into ASD cohort studies (building on NIH ASD cohorts and EPA/NIEHS children's centers)
  - Incorporate state-of-the-art exposure measurement into existing cohorts
  - Advance sensors and biomarkers for screening exposure preconception, prenatally, and in early life
  - Advance tools and methods to measure and characterize multiple stressors
  - Develop methods to assess relevant multigenerational exposures